EXHIBIT B52

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION ***THIS DOCUMENT RELATES TO ALL CASES***	**MDL NO. 16-2738 (FLW) (LHG)**

RULE 26 EXPERT REPORT OF JUDITH ZELIKOFF, PHD

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If the DNA damage cannot be repaired, the cell can self-destruct, a process called apoptosis. In cancer cells, molecules in the repair pathway are faulty. For example, a protein called p53 normally determines whether genes can be repaired or if the cell should undergo apoptosis. Many cancers have a defective version of p53, and don't repair themselves properly. Thus, cancer cells can override self-destruct signals and don't undergo apoptosis when they should.

B. Genetic Mutations

(1) ***Inherited mutations*** are passed down from parent to child and are present throughout a person's life in virtually every cell in the body. These mutations are also called germline mutations because they are present in the parent's egg or sperm (germ) cells. When an egg and a sperm cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells.

(2) A genetic predisposition (sometimes also called genetic susceptibility) is an increased likelihood of developing a particular disease based on a person's genetic makeup. A genetic predisposition results from specific genetic variations that are often inherited from a parent. These genetic changes contribute to the development of a disease, but do not directly cause it. For example, mutations in the *BRCA* gene result in an increased risk for ovarian cancer. (3) Some people with a predisposing genetic variation will never get the disease while others will, even within the same family. Genetic variations can have large or small effects on the likelihood of developing a particular disease. (4) Although each of these variations only slightly increases a person's risk, having changes in several different genes may combine to increase disease risk significantly. Changes in many genes, each with a small effect, may underlie susceptibility to many common diseases, including cancer.

(5) In people with a genetic predisposition, the risk of disease can depend on multiple factors in addition to an identified genetic change. These include other genetic factors (sometimes called modifiers) as well as lifestyle and environmental factors. Diseases that are caused by a combination of factors are described as multifactorial. (6) Most disease-causing gene mutations are uncommon in the general population. However, other genetic changes occur more frequently. Genetic alterations that occur in more than 1 percent of the population are called polymorphisms.

(7) ***Acquired (or somatic) mutations*** occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, chemical exposure, or can occur if an error is made as DNA copies itself during cell division. Acquired mutations in somatic cells (other than sperm and egg cells) cannot be passed to the next generation.

Environmental and occupational exposures to natural substances, as well as man-made chemical and physical agents, play a causative role in human cancer. Acquisition of cancer-specific alterations may be triggered by the mutational and/or non-mutational (i.e., epigenetic) events in the genome which, in turn, affect gene expression and downstream phenotypes including persistent proliferative signaling, resistance to cell death, evasion of growth suppression, replicative immortality, inflammatory response,

Help Me Understand Genetics

Mutations and Health

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What is a gene mutation and how do mutations occur?

A gene mutation is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations range in size; they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene mutations can be classified in two major ways:

- Hereditary mutations are inherited from a parent and are present throughout a person's life in virtually every cell in the body. These mutations are also called germline mutations because they are present in the parent's egg or sperm cells, which are also called germ cells. When an egg and a sperm cell unite, the resulting fertilized egg cell receives DNA from both parents. If this DNA has a mutation, the child that grows from the fertilized egg will have the mutation in each of his or her cells.
- Acquired (or somatic) mutations occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.

Genetic changes that are described as de novo (new) mutations can be either hereditary or somatic. In some cases, the mutation occurs in a person's egg or sperm cell but is not present in any of the person's other cells. In other cases, the mutation occurs in the fertilized egg shortly after the egg and sperm cells unite. (It is often impossible to tell exactly when a de novo mutation happened.) As the fertilized egg divides, each resulting cell in the growing embryo will have the mutation. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell in the body but the parents do not, and there is no family history of the disorder.

Somatic mutations that happen in a single cell early in embryonic development can lead to a situation called mosaicism. These genetic changes are not present in a parent's egg or sperm cells, or in the fertilized egg, but happen a bit later when the embryo includes several cells. As all the cells divide during growth and development, cells that arise from the cell with the altered gene will have the mutation, while other cells will not. Depending on the mutation and how many cells are affected, mosaicism may or may not cause health problems.

(6) Most disease-causing gene mutations are uncommon in the general population. However, other genetic changes occur more frequently. Genetic alterations that occur in more than 1 percent of the population are called polymorphisms. They are common enough to be considered a normal variation in the DNA. Polymorphisms are responsible for many of the normal differences between people such as eye color, hair color, and blood type. Although many polymorphisms have no negative effects on a person's health, some of these variations may influence the risk of developing certain disorders.

For more information about mutations:

The Centre for Genetics Education provides a fact sheet discussing variations in the genetic code (http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-2-variations-in-the-genetic-code).

More basic information about genetic mutations (https://geneed.nlm.nih.gov/topic_subtopic.php?tid=142&sid=145) is available from GeneEd.

Additional information about genetic alterations is available from the University of Utah fact sheet "What is Mutation?" (http://learn.genetics.utah.edu/content/basics/mutation/)

What does it mean to have a genetic predisposition to a disease?

(2) A genetic predisposition (sometimes also called genetic susceptibility) is an increased likelihood of developing a particular disease based on a person's genetic makeup. A genetic predisposition results from specific genetic variations that are often inherited from a parent. These genetic changes contribute to the development of a disease but do not directly cause it. Some people with a (3) predisposing genetic variation will never get the disease while others will, even within the same family.

Genetic variations can have large or small effects on the likelihood of developing a particular disease. For example, certain mutations in the *BRCA1* or *BRCA2* genes greatly increase a person's risk of developing breast cancer and ovarian cancer. Variations in other genes, such as *BARD1* and *BRIP1*, also increase breast cancer risk, but the contribution of these genetic changes to a person's overall risk appears to be much smaller.

Current research is focused on identifying genetic changes that have a small effect on disease risk but are common in the general population. Although each (4) of these variations only slightly increases a person's risk, having changes in several different genes may combine to increase disease risk significantly. Changes in many genes, each with a small effect, may underlie susceptibility to many common diseases, including cancer, obesity, diabetes, heart disease, and mental illness.

(5) In people with a genetic predisposition, the risk of disease can depend on multiple factors in addition to an identified genetic change. These include other genetic factors (sometimes called modifiers) as well as lifestyle and environmental factors. Diseases that are caused by a combination of factors are described as multifactorial on page 35. Although a person's genetic makeup cannot be altered, some lifestyle and environmental modifications (such as having more frequent disease screenings and maintaining a healthy weight) may be able to reduce disease risk in people with a genetic predisposition.

For more information about genetic predisposition to disease:

The World Health Organization offers information about genetic predisposition to several common diseases (http://www.who.int/genomics/public/geneticdiseases/en/index3.html), including cancer, diabetes, cardiovascular disease, and asthma.

The Genetic Science Learning Center at the University of Utah provides more information about calculating the risk of genetic diseases and predicting